

- d) inoculating cells from said monolayer into a plurality of segregated sites, and at least one untreated control site, in reproducible numbers;
- e) treating each of said plurality of segregated sites with a treating means, determining cell number relative to said at least one untreated control site, followed by correlating the chemosensitivity of the cells in said plurality of sites to concentration of exposure to said treating means in order to assess the chemosensitivity of the patient cells; and
- f) assessing the chemosensitivity of the cells in said plurality of sites for cellular markers, secreted factors, or tumor antigens.

REMARKS

Claims 33 and 34 have been amended. Claims 25 and 27-36 remain in the application. Reexamination and reconsideration of the application as amended are requested.

The Examiner has provisionally rejected claims 25 and 27-36 under the doctrine of obviousness double patenting. Applicant herewith files a terminal disclaimer in compliance with 37 CFR 1.321(c) to limit the term of the patent issuing from the current application to the term of U.S. Patent No. 5,728,541, issuing from U.S. Patent Application Serial No. 08/679,056, and any patent issuing from U.S. Patent Application Serial No. 09/095,993. Besides these, there are no other related pending applications.

The Examiner has rejected claims 25 and 27-36 under 35 U.S.C. § 112, second paragraph, for indefiniteness. The Examiner asserts that, in claim 33(e), the treating of sites with treating means is not related to chemosensitivity, no determining takes place before and after treating, and correlating chemosensitivity cannot be understood. Claim 33 states that each of a plurality of segregated sites is treated with a treating means. Claim 33 has been amended to state

that the chemosensitivity of the cells in a plurality of sites is correlated to the concentration of exposure to at least one treating means. The relationship of treatment to chemosensitivity is therefore that each of the sites is treated with a treating means, the cells in each of the sites respond to a particular concentration of exposure to the treating means, and the cells in each of the sites exhibit a chemosensitivity that can be determined by counting the number of cells present and can be correlated to the concentration of exposure to the treating means. The relationship between cell count and chemosensitivity is described on p. 12, lines 2-15 of the specification. The concentration of exposure bringing about the response is described on p. 12, line 5 of the specification.

The number of cells in each site is determined before and after the treatment. Before treatment, the determination is the result of procedures ensuring that a reproducible cell number is delivered to each row in a plate and/or a series of plates. These procedures are described on p. 9, lines 27-34 of the specification, and claims 33 and 34 have been amended to state that these procedures occur before treatment. After treatment, the determination (referred to as such in the claim) involves counting the cells in the wells exposed to the treatment and counting the cells in wells not exposed to the treatment. Claims 33 and 34 have been amended to state that the control sites are not exposed to the treatment, as is stated on p. 11, lines 9-13 of the specification. The counting process is described on p. 12, lines 2-10 of the specification.

The Examiner asserts that claim 34(e) does not set forth what is correlated with what. Claim 34(e) has been amended to state that chemosensitivity of the cells (derived from the number of cells present after treatment in relation to the number of cells present in wells not exposed to the treatment) is correlated to concentration of exposure to the treating means.

For these reasons, the Examiner's objections have been overcome. Therefore, it is submitted that the claims are in condition for allowance. Reconsideration and withdrawal of the rejections is requested. Allowance of claims 25 and 27-36 is respectfully requested.

Respectfully submitted,

WEBB ZIESENHEIM LOGSDON
ORKIN & HANSON, P.C.

By 

Barbara E. Johnson

Registration No. 31,198

Attorney for Applicant

700 Koppers Building

436 Seventh Avenue

Pittsburgh, PA 15219-1818

Telephone No. 412/471-8815

Facsimile No. 412/471-4094

MARKED-UP COPY OF CLAIMS 33 and 34:

33. (Once Amended) A method for assessing chemosensitivity of malignant or hyperproliferative cells consisting essentially of the steps of:

- a) harvesting a specimen of a patient's tissue or cells;
- b) separating mechanically said specimen into cohesive multicellular particulates with a particle size distribution between about 0.25 mm^3 and about 1.5 mm^3 ;
- c) growing a tissue culture monolayer from said cohesive multicellular particulates;
- d) inoculating cells from said monolayer into a plurality of segregated sites and at least one untreated control site in reproducible numbers; and
- e) treating each of said plurality of segregated sites with a treating means, determining cell number in each of said plurality of segregated sites relative to said at least one untreated control site, followed by correlating chemosensitivity of the cells in said plurality of sites to concentration of exposure to said at least one treating means.

34. (Once Amended) A method for assessing chemosensitivity of malignant or hyperproliferative patient cells comprising the steps of:

- a) harvesting a specimen of a patient's tissue or cells;
- b) mechanically separating said specimen into cohesive multicellular particulates having a particle size distribution between about 0.25 and about 1.5 mm^3 with avoidance of further size reduction of the particles thereafter;
- c) growing a tissue culture monolayer from said cohesive multicellular particulates;

d) inoculating cells from said monolayer into a plurality of segregated sites, and at least one untreated control site, in reproducible numbers; ?

e) treating each of said plurality of segregated sites with a treating means, determining cell number relative to said at least one untreated control site, followed by correlating the chemosensitivity of the cells in said plurality of sites to concentration of exposure to said treating means in order to assess the chemosensitivity of the patient cells; and

f) assessing the chemosensitivity of the cells in said plurality of sites[, at least one of which sites further constitutes a control site,] for cellular markers, secreted factors, or tumor antigens.